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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE
DISEASES OF INFANTS AND CHILDREN
JOHN FITCH LANDON, M.D., Editor

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1. Miller, J. B., and Boyer, E. H.: *Jour. Pediat.*, 40:767, June, 1952.
2. Ravenel, S. F.: *J.A.M.A.*, 151:707, Feb. 28, 1953.
3. Sadove, M. S.: Meeting of the Champaign County Medical Society, Champaign, Ill., March 12, 1953.

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1. Grayzel, H. G., Heimer, C. B., and Grayzel, R. W.: New York St. J. M. 53:2233, 1953.
2. Heimer, C. B., Grayzel, H. G., and Kramer, B.: Archives of Pediatrics 68:382, 1951.
3. Behrman, H. T., Combes, F. C., Bobroff, A., and Leviticus, R.: Ind. Med. & Surgergy. 18:512, 1949.
4. Turell, R.: New York St. J. M. 50:2282, 1950.

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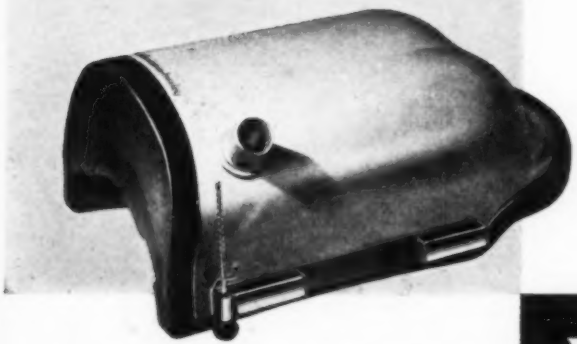

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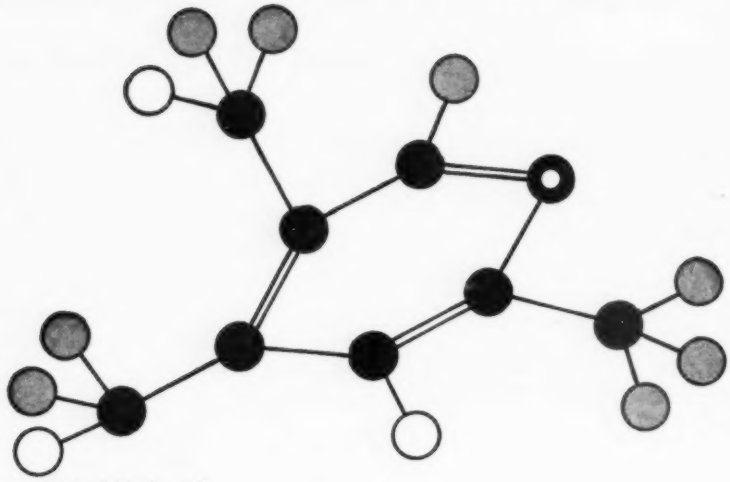

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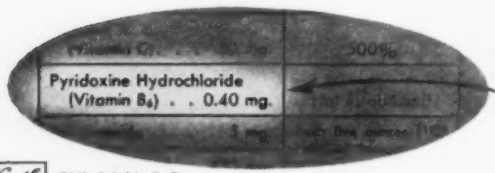

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(b) *Peel oil content significantly lower:* Samples of orange juice, home-squeezed by typical housewives, showed contents of peel oil, a cause of allergic response and poor tolerance, especially in infants, were up to 700% higher than in MINUTE MAID!

(c) *Bacterial counts dramatically lower:* Bacterial counts were found to be as high as 350,000 per ml. in home-squeezed samples, but were uniformly low in MINUTE MAID.

Since publication of the above findings, more and more physicians are recommending MINUTE MAID Fresh-Frozen Orange Juice in place of home-squeezed orange juice where optimum year-around intake of natural Vitamin C is indicated.

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New Assays Reaffirm Dietary Advantages of Minute Maid Fresh-Frozen Orange Juice on a Cost Basis

A second report comparing the individual mineral and vitamin values of MINUTE MAID Fresh-Frozen Orange Juice and home-squeezed juice of the same type oranges has recently been published.

In this latest study, each sample was analyzed separately. The analyses showed that MINUTE MAID Fresh-Frozen Orange Juice was equal to, or superior to, the home-squeezed juice in *all* of the components listed below:

TABLE

Mean Values in Samples Tested

COMPONENT	UNITS	MINUTE MAID FRESH-FROZEN ORANGE JUICE	HOME-SQUEEZED ORANGE JUICE
Betaine	mg./100 ml.	49	46
Biotin	mcg./100 ml.	0.26	0.26
Choline	mg./100 ml.	12	12
Cobalt	mcg./100 ml.	74	67
Folic acid	mcg./100 ml.	2.2	2.2
Iodine	mcg./100 ml.	0.24	0.21
Manganese	mcg./100 ml.	33	18
Nitrogen			
Total	mg./100 ml.	104	79
Amino	mg./100 ml.	22	22
Volatile	mg./100 ml.	8	7
Non-volatile	mg./100 ml.	96	72
Pantothenic acid	mcg./100 ml.	146	145
Para-amino-benzoic acid	mcg./100 ml.	4	4
Phosphorus	mg./100 ml.	19	18
Potassium	mg./100 ml.	380	290
Riboflavin	mcg./100 ml.	18	17
Tocopherols	mg./100 ml.	107	104
Vitamin A	mcg./100 ml.	19	16
Thiamine	mcg./100 ml.	87	83
Vitamin B_{12}	mcg./100 ml.	0.0022	0.0012

Although the results are again susceptible to variation according to crop and year, Fresh-Frozen MINUTE MAID was equal to the home-squeezed juice in the samples tested for the largest number of components listed; and in the mean values for iodine, manganese, potassium, Vitamins A and B_{12}, MINUTE MAID showed appreciably *higher* values.

SUMMARY

These new findings help enlarge professional knowledge of the nutrient constituents of orange juice in general and add fresh evidence that, on a cost basis, MINUTE MAID Fresh-Frozen Orange Juice has significant dietary advantages. Penny for penny, MINUTE MAID offers not only *more* Vitamin C, but also *more* of all the other vitamins and minerals listed than home-squeezed orange juice.

Taken in conjunction with the previously published findings, this should confirm the choice of physicians who recommend MINUTE MAID in place of home-squeezed orange juice.

REFERENCES:

(1) Rakieten, M. L., *et al.*, Journal of the American Dietetic Association, October, 1951.
(2) Joslin, C. L., and Bradley, J. E., Journal of Pediatrics, Vol. 39, No. 3, pp. 325-329 (1951).
(3) Rakieten, M. L., *et al.*, Journal of the American Dietetic Association, November, 1952.
(4) Assn. Official Agricultural Chemists: Methods of Analysis, 7th ed. Washington: Assn. Off. Agric. Chemists, 1950.

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PROGERIA*

REVIEW OF THE LITERATURE WITH REPORT OF A CASE

MAMDOUH GABR, M.B., D.Ch., M.D.
Cairo, Egypt.

Progeria is a term suggested by Gilford in 1904 to a syndrome which was first described by Hutchinson in 1886 under the name "congenital absence of hair and mammary glands with atrophic condition of the skin and its appendages" (Hutchinson 1886).

Since those original publications, relatively few cases have been reported, which present the same features of the disease as described by Gilford. The term progeria, however, was vaguely used to describe various syndromes in which premature senility was a feature such as Werner's syndrome, (Thannhauser, 1945; Shelby and Vaughan, 1951), mental deficiency with premature senility (Moehlig, 1946; Wilkins, 1950; Neill and Dingwall, 1950), Simmond's cachexia in children, etc. Most late workers, however, felt it necessary to restrict the term "progeria" to the classical syndrome of Hutchinson-Gilford (Thomson and Forfar, 1950; Cooke, 1953). Thomson and Forfar, in 1950, excluded 25 cases described by different authors as progeria or progeria-like syndromes, and they found only 18 typical cases reported in the literature until that time. Wilkins in his text, "The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence" described a case belonging to Dr. James C. Hughes, in 1950. Cooke, in 1953, added a further case, bringing the total number of reported typical

*From the Pediatric Department, Kasr El-Aini Faculty of Medicine, Cairo, Egypt.

cases to twenty-one. Schondel's second case (1943) and Moehlig's case (1946), included in Cooke's series, cannot be considered typical. Keith, in 1913, described the skeleton of a previous case. Thomson and Forfar (1950) refer to an unpublished case by Paterson and Ebbs.

Clinical Features. Cases of progeria have been reported from all over the world. Of the 21 typical cases recorded, five were reported from U. S. A. (including one negro boy), three from England, 10 from the Continent, one from Argentina and one from Tunis (Table 1). The case to be presented is the first case reported from Egypt. No definite familial or hereditary cases were reported. Due to the similarity of reported cases, a standard clinical picture of the disease can be readily summarized.

TABLE 1.

	Author	Year	Sex	Age	Wt.	Ht.	Age at Death
1.	Hutchinson	1886	M	15	17.2	109	17
2.	Gilford	1897	M	14	16.3	104	18
3.	Variot & Pironneau	1910	F	15	11.6	102	15
4.	Schippers	1916	M	26	15.6	115	26
5.	Oricco	1918	M	19	15.4	113	21
6.	Nasso	1925	F	4½	...	83	..
7.	Curtin & Kotzen	1929	F	7	11.8	96	9
8.	Strunz	1929	F	6½	9.4	90	..
9.	Thiers & Nahan	1933	M	19	23.2	131	..
10.	Schiff	1934	F	4	16.6	100	..
11.	Exchaquet	1935	F	14	12.9	113	..
12.	Broc et al.	1935	M	11	14.0	116	..
13.	Popek & Hadlik	1938	F	8	11.2	99	..
14.	Mitchell & Goltman	1940	F	10	12.7	105	..
15.	Zeder	1940	M	5	7.6	83	..
16.	Schondel	1943	F	5½	10.9	93	..
17.	Talbot et al.	1945	M	6	10.9	95	7
18.	Schwartz & Cooke	1945	M	5	9.8	83	8
19.	Thomson & Forfar	1950	M	4½	9.0	89	..
20.	Hughes	1950	M	5	11.0	89	..
21.	Cooke	1953	M	13	13.2	110	13

Sex incidence is almost equal. The affected patient is usually normal at birth, although slightly under-weight. The condition manifests itself at the end of the first year by loss of hair and later failure to grow both in weight and in height. The growth curves in all reported cases are almost identical. After an almost normal increase during the first year, the weight becomes stabilized and

thereafter remains in the zone of a normal child in the second or third year (about 15 kgms.). Similarly the height increases slowly but regularly during the first decade to reach eventually the normal 4-5 years range (about 110 cms.). (Cooke, 1953). Intelligence is always normal or above normal. Sitting, standing and walking may occur at the normal time, but teeth eruption is usually delayed.

When the full blown picture of the disease is established, all progeric patients strikingly look alike. The progeric child is bald apart from few fluffy hairs usually on the vertex. Dilated scalp veins are evident and sometimes a venous hum is heard over the skull (Thomson and Forfar, 1950; Talbot et al., 1945). The head looks large in relation to the small face. The anterior fontanelle is usually opened but may be closed, while deficient ossification of the bones of the posterior part of the skull has been reported in several cases (Thiers and Nahan, 1933; Broc et al., 1935; Hughes, 1950). An appearance of double chin is sometimes present, due to the enlarged submaxillary glands and the markedly retracted chin. The eyes appear prominent, due to the small orbital cavities. The eyebrows and eyelashes are lost. The palate is usually highly arched and the mandible small and micrognathios so that it is often difficult to examine the child's throat. The tongue is small and the teeth are overcrowded. The nose is beak-like with the nasal cartilages shining through the thin skin. The ears stand out, but the lobules are usually atrophied. The thoracic inlet is narrow, due to the very small clavicles. The mammary glands are usually atrophied. The abdomen is protruberent, the umblicus being flattened and the liver sometimes markedly enlarged. The genitalia are usually normal, but in the few older children reported, there is no evidence of sexual maturity. The limbs are thin and slender with enlargement of the joints, especially the knees, wrists and interphalangeal joints. There is limitation of movement of the joints resulting in the characteristic stooping attitude and the straddling gait. The skin is thin and characterized by loss of subcutaneous fat all over the body; although it is often retained in the pubic region and cheeks in early childhood. Sclerodermic-like changes are reported and a fine brown pigmentation is common. Sweat glands are present, but the hair follicles are very scarce. The nails are in most cases atrophied, transverse, furrowed and may be even

absent. The condition of the skin and the stooping posture give the child the characteristic elderly appearance.

Arteriosclerotic changes supervene in all cases as early as the fifth year. Angina is common and the blood pressure is usually raised. The heart may enlarge, and a systolic murmur over the apex is common. Hemiplegia occurred in two cases. Arthritic changes in the joints were reported to occur as early as the sixth year. Death usually results from coronary thrombosis, the average age of death being 16 years (varying from 7-26 years).

Investigations reveal a normal blood picture; sometimes the erythrocyte sedimentation rate is raised. The blood urea is slightly raised, and the blood cholesterol is often high. Blood phosphorus and calcium are usually normal, although two cases of hypercalcaemia have been reported (Exchaquet, 1935; Zeder, 1940). The Wassermann reaction has only once been reported to be positive (Orrico, 1918). The basal metabolic rate is usually high and a raised creatine-creatinine ratio has been reported (Thomson and Forfar, 1950). The serum potassium, sodium, protein, iodine, sugar and phosphotase are normal. The urine shows no change and urinary 17-ketoteroids are usually within normal limits. The electrocardiogram shows no definite changes, unless coronary affection is present.

Radiologically the following features are characteristic of progeria: the small face, small mandible, almost passing in a straight line from the feebly developed chin to the auditory meatus; bilateral coxa valgae; small clavicles and ovoid notched vertebrae with a fish mouth appearance. Certain other radiological features are also often present: a persistent anterior fontanelle and deficient ossification of posterior cranial bones. The sella turcica was reported to be enlarged in three cases only (Exchaquet, 1935; Zeder, 1940; Thomson and Forfar, 1950). There is generalized rarefaction of all bones. The osseous age usualy corresponds to the chronological age but may be delayed or advanced occasionally.

Necropsy was carried out on four of the nine patients who were followed to death. All cases showed advanced arteriosclerotic manifestations with its sequelae. The thymus was persistent in two cases (Gilford, 1904; Talbot et al., 1945), the thyroid small in two cases (Orrico, 1918; Manchot, 1940), the parathyroids were small or even absent in three cases (Orrico, 1918; Manchot, 1940; Talbot

et al., 1945) and the adrenals were atrophied in two cases (Gilford, 1904; Orrico, 1918). The pituitary was slightly small in two cases (Orrico, 1918; Manchot, 1940) and larger than normal in one case (Talbot et al., 1945).

Owing to the clear-cut picture of the condition, no other disease can resemble it. Hereditary ectodermal dysplasia is a rare congential abnormality, affecting the ectodermal structures only, resulting in alopecia, lack of sweating and absence of teeth. It thus bears a superficial resemblance to the condition but is easily excluded (Harris, 1927). The presence of premature senile changes in mentally defective children is occasionally reported (Neil and Dingwall, 1950; Wilkins, 1950; Moehlig, 1946). In fact, the first case of premature senility reported, the famous French dwarf, Bébé, was a microcephalic idiot (Gilford, 1904). Such cases should not be considered as true examples of progeria.

Various hormones were tried for treatment. Testosterone is said to be the most promising, but results are not encouraging (Talbot et al., 1945; Moehlig, 1946). An attempt to diminish the high basal metabolic rate by thiouracil was reported, but was also a failure (Talbot et al., 1945). Cortisone was recently tried in a case (Rossi, 1951), but was reported to be ineffective.

CASE REPORT

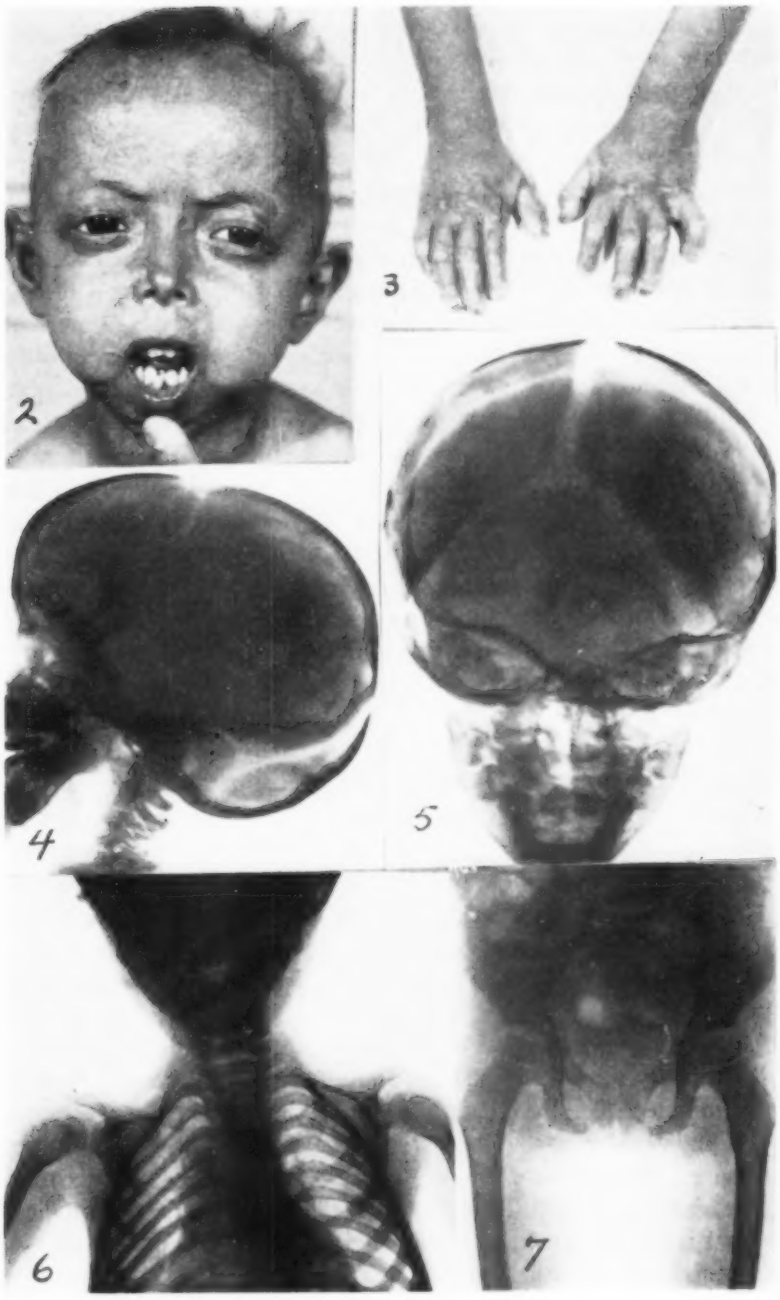
The patient, A. M., first came under our observation in September 20, 1952 when she was four years old. Her mother brought her to the hospital on account of her baldness and arrested growth. She was previously admitted to hospital when two years old with the diagnosis of marasmus. The mother gave birth to six children; two died from intercurrent infections. The patient, A. M., is the fourth child. Both parents and all children were examined, and, apart from the younger child, N. M., to be referred to later, none showed any special abnormality related to the disease.

A. M. was a full term child. At birth she looked absolutely normal in appearance as well as in weight. She was breast fed and showed no feeding difficulty. She sat unsupported at the age of seven months. Walking, however, was delayed until the age two years. Teeth eruption was also delayed; the first tooth appeared at one and one-half years. Her mentality was described by her mother to be normal. She described her girl as well tem-

pered and wise. She reported no special malady in the past history of the child. Stunting of growth was first noticed at the age of two years and thereafter growth was described by the mother to be almost arrested. Her scalp hair was normal until the age of seven months when it gradually fell away. At the age of two years her eyelashes disappeared and her eyebrows became scanty.

Patient A.M. Sister of A.M.

Examination revealed a small statured emaciated baby with a high pitched voice, intelligent look and elderly face (Fig. 1). Her stooping posture was characteristic, showing the flexion attitude of all her joints. Her measurements revealed a marked arrest of growth: Weight 8.25 kgms, (normal for the age 16.5 kgms); height 76 cms. (normal 103 cms.); skull to symphysis 44 cms. and symphysis to feet 32 cms.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Her head looked big in relation to her body but this was only apparent since her skull circumference was 46.5 cms., which was less than the normal for her age (average normal at four years 50.8 cms.). The anterior fontanelle was one centimeter open. Apart from a tuft of tawny hair on the vertex she was bald. Dilated scalp veins shined through the thin stretched skin. Her face was small. Her eyes were slanting downwards and outwards with complete absence of eyelashes and only a few fine hairs at the site of her eybrows. Her nose was small with a flattened bridge and anteriorly facing external nares. The ears were of normal size and shape. The mouth was small with a characteristically small receding lower jaw which gave the appearance of a double chin. The teeth were all present but the lower incisors were crowded (Fig. 2). The tongue was small and the palate was highly arched. The mouth could not be opened sufficiently for an examination of the throat. The thyroid was normal in size.

The thorax was conical in shape with a very narrow thoracic inlet, due to the rudimentary clavicles. The clavicles were only developed in their sternal ends while a fibrous band replaced the rest of the bones thus making it possible to bring the patient's shoulders anteriorly almost to touch each other. The nipples were small but present.

The limbs were thin with a relative enlargement of the joints, specially the knees and knuckles. All the joints showed a flexion attitude and limited extension, specially in the interphalangeal joints. This flexion attitude of the knees, hips and spine accounted for her characteristic bent posture. Her gait, however, was normal. The hands were senile in appearance with glazing stretched skin, square tipped fingers and small slightly atrophied nails, which were more transverse than longitudinal. Her toe nails showed the same picture (Fig. 3).

A complete examination of the internal organs revealed no abnormality. Both lungs were free, her respiratory rate was 28 per minute. The apex beat was in the fourth space in the nipple line and the heart sounds were normal. The pulse was 100 per minute. Her blood pressure was 108 systolic and 25 diastolic. The abdomen was full but not markedly distended; the umbilicus was slightly protuberant. The fat over the abdominal wall was 0.5 cms. thick, but the suprapubic pad of fat was present. The liver

was of normal size, and the spleen was not palpable. The genitalia were of normal development for her age. The central nervous system was normal in all respects.

The condition of her skin was reported by Dr. Zawahry as follows: "The scalp shows alopecia mainly marginal, occipital and temporal. The existing hair is harsh and short. The skin as a whole is harsh and dry. It is icthyotic, the icthyosis mainly evident on the limbs. A sclerodermic element is present, specially on the fingers (sclerodactyly). The nails are more transverse than longitudinal and are partially atrophied."

Investigations. Blood: Haemoglobin 75 per cent, R.B.C. 3,900,000, W.B.C. 9,200, polymorphs. 50, lymphocytes 50. E.S.R. 60 mm. per hour.

Blood urea: 41 mgm. per 100 cc. of blood. Blood sugar (fasting) 90 mgm. per cent.

Blood calcium 11 mgm. per cent. Blood phosphorus 4 mgm. per cent.

Blood cholesterol 185 mgm. per cent, Wassermann negative.

Urine: Amount per 24 hours 870 cc. Specific gravity 1010.

Urea per 24 hours, 12 gms. No albumin, sugar or casts. 17 ketosteroids per 24 hours' urine, 0.5 mgm.

Stools: Negative for parasites.

The electrocardiogram tracing showed no abnormality.

Fundi showed choroidal regeneration on both sides.

Radiological Examinations. X-ray of skull (Figs. 4 and 5) revealed thinness of cranial bones, defective ossification of the bones in the posterior part of the cranium, small maxillae and small mandible with overcrowded teeth. The sella turcica was normal.

X-ray of the chest showed the characteristic pyriform shape of the thorax. The very thin rudimentary sternal ends of the clavicles were hardly seen (Fig. 6). The heart was normal and there was no radiological evidence of a persistent thymus.

Bilateral coxa valga was evident in the x-ray of the pelvis (Fig. 7.).

The vertebrae showed persistence of the ovoid notched infantile pattern (fish mouth appearance).

X-ray examination of the limbs revealed generalized osteoporosis. The ossification centres correspond with the age of 3-4 years.

A brief account of the patient's youngest sister N.M. will be given, since she presented few features resembling her sister's condition:

N.M. was nine-months-old when examined with her sister. The mother gave the following history: She was full term and born in a good general condition. At the age of five months the mother became anxious about her condition since she lost most of her hair. Apart from this the mother reported the infant to be normal in all respects and to her mind grew normally. She sat unsupported at the age of seven months. Examination revealed a small infant weighing 5.5 kgms. (normal for her age 8.5 kgms.). Her height was 69 cms., which was normal for her age. She could sit alone unsupported. Dr. Zawahry commented on her skin condition as follows:

"Her scalp shows partial alopecia mainly in the occipital region and she exhibits some hardness and dryness of the skin specially over the extensor surface of the upper limbs." X-ray of her skull showed a persistent post-fontanelle. Her chronological age as judged by the carpal bones was advanced corresponding to the age of two years. X-ray of the pelvis showed evidence of coxa valga. Apart from these features she shared no other feature of the disease with her sister.

COMMENT

The reported case showed all the classical features of progeria, viz., dwarfism, senile appearance, loss of hair, micrognathios, small clavicles and coxa valga. The skin manifestations were very advanced, the sclerodermic element being specially evident. Apart from the slight increase in blood pressure and in the blood urea in the presented case; there was no evidence of cardiovascular involvement. This is probably due to the young age of the patient.

A marked feature of the case was the deficient calcification of the skull base, the widely opened fontanelle and the rudimentary clavicles which were almost unossified. These are all features of cleidocranial dysostosis. This condition was also present in three other reported cases (Thiers and Nahan, 1933; Broc et al., 1935; Hughes, 1950). It is interesting to note that in the x-ray picture of Broc's patient the clavicles were not apparent although there was no mention of their condition in the text.

The condition of the younger sister of this patient raises the question of heredity. It is generally agreed that progeria is not a heredofamilial condition; but a thorough review of the literature shows that in Hutchinson's case the mother had alopecia while in Thomson and Forfar's case the father had a poorly developed chin. The possibility that the condition may be recessively inherited has to be considered. It is to be recalled, in this respect, that cleidocranial dysostosis, which is present in 3 cases as well as in the present case, is a heredofamilial disease. It is also to be mentioned that Werner's syndrome, which has a high family incidence, is considered to be an adult type of progeria (Thannhauser, 1945). Thannhauser suggests that progeria of children and Werner's syndrome of adults result from multiple germ plasm defects manifesting themselves at different ages. A follow-up of the younger sister's condition may be of great help in this respect.

Owing to the rarity of the cases, the etiology of the disease remains obscure. Nearly every endocrine gland has been blamed to be responsible for the condition. Many authors speculated that pituitary dysfunction was the causative factor, other endocrine glands, especially the parathyroids, being secondarily affected. Such theories lend support from the few incomplete autopsies reported, which showed atrophy of the pituitary or parathyroid glands. The clinical picture of the disease, however, shows no resemblance to any known endocrine syndrome. There is undoubtedly a congenital factor affecting all three germinal layers, ectoderm, mesoderm and endoderm, causing arrest of growth associated with premature senile manifestations. It has to be admitted that such a factor is still unknown.

SUMMARY

A thorough review of the literature on progeria shows that twenty-one typical cases were reported until 1953. A classical case showing all the manifestations of the disease is described. The patient's younger sister shows some of the manifestations of the disease. The possibility of an heredofamilial factor is discussed. The etiology of the disease is considered to be still obscure.

REFERENCES

Broc, R.; Nicolle, M. and de Beaujeau, A. V.: Presse med., 43: 786, 1935.
Cooke, J. V.: J. Pediat., 42: 26, 1953.
Exchaquet, L.: Rev. franc. de pediat., 11: 467, 1935.

Gilford, H.: Practitioner, 73:188, 1904.
Harris, C. F.: Proc. Roy. Soc. Med., 21: 227, 1927-28.
Hughes, J. C.: Endocrine Disorders in Childhood and Adolescence. Ed. Wilkins, L., p. 136, 1950.
Hutchinson, J.: Tr. Med. Chir. Soc., Edinburgh, 69: 473, 1886.
Keith, A.: Lancet, 1: 305, 1913.
Manchot, W. A.: Nederl. tijdschr, v. geneesk., 84: 3774, 1940.
Moehlig, R. C.: J.A.M.A., 132: 640, 1946.
Neill, C. A. and Dingwall, M. M.: Arch. Dis. Childhood, 25: 213, 1950.
Orrico, J.: Prensa med. argent, 5: 133, 1918.
Rossi, E.: Helvet. paediet. acta, 612: 165, 1951.
Shelby, D. C. and Vaughan, J. O.: J. Pediat., 38: 559, 1951.
Schondel, A.: Acta paediat., 30: 286, 1943.
Talbot, N. B.; Butler, A. M.; Pratt, E. L.; MacLachlan, E. A. and Thannheimer, J.: Am. J. Dis. Child., 69: 267, 1945.
Thannhauser, S J.: Ann. Int. Med., 23: 559, 1945.
Thiers, J. and Nathan: J. de radiol. et d'électrol., 17: 675, 1933.
Tomson, J. and Forfar, J. O.: Arch. Dis. Childhood, 25: 224, 1950.
Wilkins, L.: Endocrine Disorders in Childhood and Adolescence, p. 137, 1950.
Zeder, E.: Monatschr. f. Kinderh., 81: 167, 1940.

INCREASED LEAD ABSORPTION RESULTING FROM PICA. (Maandschrift voor Kindergeneeskunde, Leyden, 21:128, April 1953). A 7-year-old boy had severe hypochromic microcytic anemia, splenomegaly, and gastric achylia. For three years the boy had repeatedly eaten lead paint. Signs of malnutrition had existed for a long time. Despite the pica (eating of lead) the boy showed no symptoms of lead poisoning. In this connection, the authors stress the difference between increased lead absorption and lead poisoning. The latter is usually characterized by encephalopathy, neuritis, paralysis, and intestinal colics. None of these symptoms were present in the boy. His severe anemia might have been caused by the lead intake or by deficient nutrition. It is unlikely that the achlorhydria was the only cause of his hypochromic anemia. Possibly intestinal disturbances were partially responsible. Psychic factors may also have played a part, and these in turn may have caused anorexia, with the result of deficient food intake, so that a vicious circle was created. It is difficult to say which factor was primary. Achlorhydria combined with hyperchromic anemia occurs oftenest in women. Women with chlorosis frequently have pica.—*Journal A.M.A.*

PATHOGENESIS OF MONGOLISM FOLLOWING MATERNAL ILLNESS; ROLE OF ADRENALS

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While the pathogenesis of mongolism is uncertain, increasing numbers of cases following maternal illness are being reported. To account for the development of mongolism, this paper invokes the "target hypothesis," with the fetal adrenals as the probable target. Reasons are given for the belief that impairment of the fetal adrenals by maternal infections and by meteorologic factors results in a deceleration of growth responsible for the so-called "atavistic" characteristics seen in mongols.

The term atavism, by definition, means inheritance of a characteristic from remote ancestors. Since chimpanzee-like ears and other "atavistic" features of mongols are obviously not inherited, for mongols cannot reproduce, the term "atavism" is here used descriptively and without hereditary implication. The presence of anomalies at birth should not be construed as necessarily inherited.[1]

TARGET HYPOTHESIS

Since there have been instances of mongolism in only one of twins,[2] it has become necessary to find a factor capable of striking a "target" in one and not in the other twin. This is known as the "target hypothesis." The target must be struck at a "critical period," some time in the first three months of pregnancy. The site of the target in the embryo is unknown, but the noxa or "bullet" may be virus, toxin, anoxia or ionized air.

It is conceivable that the virus of rubella, or the toxin of rheumatic fever,* to use two known noxae as examples, may strike a "target" in one embryo, and not the other. Viruses and toxins are not distributed equally throughout the body. In rubella, the rash, presumably caused by the virus, is not uniform in the skin, but appears as macules with normal areas between; furthermore, it does not cover the entire body. In rheumatic fever and rheumatoid arthritis, toxin of the streptococcus may produce swelling and

*Gregg called attention to the arthritic complications of rubella in many pregnant women who subsequently gave birth to defective children. Simpson[3] reported a severe epidemic of rubella, in which 35 per cent of cases showed polyarthritis. Swan and Tostevin[4] mentioned eight cases of rubella with associated pain and stiffness in joints; in some cases only the knees or wrists were involved.

erythema in one wrist or ankle and leave the other joints intact. Thus, it requires but little imagination to believe that viruses or toxins may injure the target of only one twin, leaving the other intact.

Weather factors may blight the target during the critical period to produce malformation. These factors include anoxia[5, 6] and ionized air. I believe these factors may act in either of two ways—directly on the target, or indirectly by quickening bacteria in maternal foci of infection, the circulating toxins of bacteria striking the target. The combination of anoxia and heavy ionization of the atmosphere during major storms is especially conducing to exaltation of streptococci in foci of infection,[7] resulting in rheumatic pains,[8, 9] and a host of other "toxic" phenomena.[9, 10, 11] Future studies may reveal the pathogenicity of bacterial toxins on the target of the developing embryo.

The direct effect of ionized air in the production of malformations is seen under such varying conditions as x-ray irradiation of the pregnant uterus,[12, 13] atomic bombing, and during storms. Regarding the effect of atomic bombing in Hiroshima, Plummer[14] reported on a total of 205 children who had been exposed during the first half of intra-uterine life; among this number were two mongols and six microcephalics with mental retardation. The pathogenic action of heavily ionized air in major storms may be exerted during a sudden drop of barometric pressure. During summer thunderstorms barometric pressure changes are negligible, ruling out the factor of anoxia. Poultrymen well know that many or all turkey eggs fail to hatch if, during the first days of a setting, a thunderstorm occurs.[15] In this respect turkey eggs are more radiosensitive to summer storms than are hens' eggs.

ADRENALS AS TARGET ORGANS

It is not known whether there is a primary site of attack by noxae. Such a possibility is suggested by the fact that the *anlage* of certain organs which are found defective at birth may not be present at the time of the insult in early pregnancy.[4, 16] In the case of maternal rubella, these *anlage* cannot be injured "unless it is assumed that the virus of rubella may persist in the tissues for some time after its initial invasion,"[4] an unlikely presumption.

That the adrenals are the target organs is at present speculative,

but this possibility should be considered for three reasons: (1) the adrenal cortex controls the development of organs (brain, heart) found defective in many mongols,[17, 18] (2) congenital anomalies have been produced with cortisone which induce a subsequent cortical hypoadrenia; and (3) there is evidence in mongols of cortical hypoadrenia subsequent to birth. These points are discussed briefly.

1. *Control Exerted by Adrenal Cortex over Developing Organs.* Normal physical and cerebral development in utero seems to be dependent upon an intact adrenal cortex.[19, 20, 21] The adrenal cortex in mongols shows no pathology but is frequently immature.[19, 22] Diffuse amyelination found in the cerebrum of mongols[23] is believed by Hirning and Farber[24] to be due to insufficiency of the adrenal cortex. Even in the absence of recognizable pathology in the adrenal cortex, two possibilities remain; first, with finer staining techniques, pathology may yet be demonstrated; second, study of structure alone is not sufficient to determine function.[25] Professor Sajous recognizes a functional hypoadrenia, "a form in which the adrenals, though not the seat of organic lesions, are functionally deficient because of tardy development." He states that "deficient activity of the adrenals" may restrain the growth of neurons, "thus leaving a brain in a state of partial development which in turn entails a correspondingly marked degree of idiocy."

2. *Congential Anomalies Produced with Cortisone.* Cortisone is teratogenic when administered to pregnant animals during the early period of gestation.[26-31] In general, the earlier cortisone is injected the more severe are the defects.[26] The administration of cortisone depresses cortical function.[32] The resulting cortical hypoadrenia may well be the factor in the production of congenital anomalies.[33] Three years before the experimental defects were first produced with cortisone, I published evidence relating congenital defects following maternal rubella to fetal cortical hypoadrenia produced by rubella.[34]

3. *Cortical Hypoadrenia in Mongols.* Cortical hypoadrenia may be suspected from the following symptoms present in mongols: lack of animation at birth, hypothermia, anorexia, asthenia, hypotension, extraordinary laxity of joints and decreased muscle tone, susceptibility to infections and early demise.[24, 35]

MONGOLISM AS AN "ATAVISM"

One can hardly deny the existence of "atavistic" characteristics seen in mongols.[36, 37] There is the simian appearance, including chimpanzee lip and chimpanzee-like ear (Fig. 1), Darwin's tubercles, peculiar posture of head seen in apes, wide separation of the big toe from remaining toes, transverse fold across the whole palm in 50 per cent of cases similar to the one found in anthropoid apes, myopia, duplicated nipples,[35] and the smaller skull and brain,[17, 23] all of which suggest "atavism." Husler[38] states: "The glance from below upwards, and wry position of the head, an incongruity of the direction of vision, suggest atavism and the posture of the head as we recognize it in animals" (Figs. 1 and 2).

FIGS. 1 and 2. Wry position of head commonly seen in mongols. FIG. 1 also illustrates chimpanzee lip and chimpanzee-like ear.

Crookshank finds that cases in which the mental defect is least pronounced tend morphologically to resemble children of the Mongolian race, while severe cases of this type show characteristics that appear to be simian, and among the anthropoid apes, are peculiar to or most noticeable in the orang. In this connection consider the phylogenetic and evolutionary implications afforded by a study of the comparative incidence of the Rh factor. This factor is found in 100 per cent of Macacus rhesus monkeys, 99.75 per cent of Japanese,[39] 99.3 per cent Chinese,[40] and in only 85 per cent of the white population.

DISCUSSION

Many theories of the causation of mongolism may readily be discarded. Heredity can be ruled out by the fact that mongols cannot reproduce.[41, 42] Other prevailing theories fail to account for the production of only one mongol among twins. These hypotheses include "exhaustion product" (Shuttleworth); "diminished viability of ova" (Jenkins[43]); "threshold condition of hormonal sterility" (Benda), and "advanced age of the mother" (Bleyer[44]). A further weakness of these theories is the fact that normal children may sometimes be born subsequently. As in many other studies,[47] advanced age of the mother seemed to be a factor in a current study presented by the writer.[45] However, further analysis of our cases revealed illness during early pregnancy, in part caused by chronic infections (sinusitis, nephritis, bronchitis, bacterial asthma, rheumatic pains) often present in aging women.

The "target hypothesis" satisfactorily explains the following three observations in mongolism: its existence in only one of twins; the apparent onset at the "critical period"; and the frequently associated defects which have their onset at this critical period. The increasing frequency of cases of mongolism with a history of maternal illness at the critical period places the "target hypothesis" without a rival at the present time.

If any noxa strikes the target organ during the "critical period," in the second or third month of pregnancy, the "atavism" or deceleration toward mongolism may begin. Ontogenesis is delayed and incomplete phylogeny results. Expressed in the words of others, there is a "deceleration of normal growth during the fetal period from about the sixth to the fourteenth week."[46] The development being delayed, the end-products are "unfinished children" (Shuttleworth, 1886), or in the view of Crookshank, there is "a state of infantilism of phylogenetic significance."

CONCLUSIONS

The "target hypothesis" best explains the mechanism by which maternal illness during early pregnancy is followed by the birth of a mongol. This hypothesis must be invoked to explain mongolism in one of twins.

The target may be the embryonic adrenal cortex, as inferred from its organogenetic role, from the experimental effect of corti-

sone on the embryo of pregnant animals, and from the presence in mongols of numerous hypoadrenic symptoms. The pathogenic agent may be some type of infection (virus, toxin), anoxia, or ionized air, any of which might affect the adrenal cortex of the embryo.

When the adrenals are presumably rendered defective by the toxic agent, organogenesis is delayed, retarding most seriously the development of the brain. There may be incomplete closure of cardiac septa and other defects, such as hernia, epicanthus, hypoplastic gonads, chimpanzee-like ear and simian palmar line. Ontogenesis being retarded, full phylogeny may not be achieved, resulting in non-hereditary "atavism." The "atavism" may extend to early man (racial Mongolism) and even beyond, to the simian.

REFERENCES

1. Ingalls, T. H.: Study of Congenital Anomalies by Epidemiologic Method: Consideration of Retrolental Fibroplasia as Acquired Anomaly of Fetus. New England J. Med., 243: 67, July 20, 1950.
2. Southwick, W. E.: Time and Stage in Development at Which Factors Operate to Produce Mongolism. Am. J. Dis. Child., 57: 68, Jan. 1939.
3. Simpson, R. E. H.: Rubella and Congenital Malformations. Lancet, 1: 483, April 8, 1944.
4. Swan, C. and Tostevin, A. L.: Congenital Abnormalities in Infants following Infectious Diseases during Pregnancy, with Special Reference to Rubella: A Third Series of Cases, M. J. Australia, 1: 645, May 11, 1946.
5. Stockard, C. R.: Developmental Rate and Structural Expressions: An Experimental Study of Twins, "Double Monsters" and Single Deformities, and the Interaction among Embryonic Organs During Their Origin and Development. Am. J. Anat., 28: 115, 1921.
6. Ingalls, T. H.: Mongolism. Scient. Am., Feb. 1952.
7. Brown, E. E.: Streptococcic Dissociation and Its Significance. Northwest Med., 44: 272, Sept. 1945.
8. Brown, E. E. and Wasson, V. P.: Capillary Resistance in Rheumatic Children. J. Pediat., 18: 328, March 1941.
9. Brown, E. E.: Cause of Cracking Joints: Relation to Weather and Fibrositis. Northwest Med., 48: 537, Aug. 1949.
10. Brown, E. E.: Focal Infection (textbook in preparation).
11. Brown, E. E.: Capillary Resistance in Scarlet Fever. ARCH. PEDIAT., 17: 553, Sept. 1940.
12. Russell, L. B.: X-ray Induced Developmental Abnormalities in Mouse and Their Use in Analysis of Embryological Patterns. 1. External and Gross Visceral Changes. J. Exper. Zool., 114: 545, 1950.
13. Warkany, J.: Etiology of Congenital Malformations. In Advances in Pediatrics. Vol. 2, p. 1, 1947.
14. Plummer, G.: Anomalies Occurring in Children Exposed In Utero to the Atomic Bomb in Hiroshima. Pediatrics, 10: 687, Dec. 1952.
15. Blair, W. R., Colonel, Signal Corps, U. S. Army, personal communication, Feb. 21, 1938. (Colonel Blair was called into consultation by the Chicago Poultryman's Institute to help solve the problem of non-hatching of eggs following thunderstorms.)
16. Carruthers, D. G.: Congenital Deaf-mutism as a Sequela of a Rubella-like Maternal Infection During Pregnancy. M. J. Australia, 1: 315, 1945.
17. Brousseau, K.: Study of Physical and Mental Characteristics of Mongolian Imbeciles, 1928.
18. Aycock, W. L. and Ingalls, T. H.: Maternal Disease as a Principle in the Epidemiology of Congenital Anomalies with a Review of Rubella. Am. J. M. Sc., 212: 366, Sept. 1946.
19. Sajous, C. E. deM.: Internal Secretions and Principles of Medicine, 8th Ed., 1919.
20. Pappenheimer, A. M.: Hypoplasia of Adrenals in Anencephaly. Proc. New York Path. Soc. 16: 165, Oct.-Nov., 1916.
21. Ilberg, cited by Pappenheimer, Ref. 20.
22. Stefko, W. H. and Ivanowa, L.: Anatomic and Pathologic Features of Mongolism. Bull. Soc. roumaine de neurol., 26: 57, 1935.

23. Davidoff, L. M.: The Brain in Mongolian Idiocy. Arch. Neurol. & Psychiat., 20: 1229, 1928.
24. Hirning, L. C. and Farber, S.: Histologic Study of Adrenal Cortex in Mongolism. Am. J. Path., 10: 435, May 1934.
25. The Changing Concepts in Pathology. Editorial, J.A.M.A., 120: 375, Oct. 3, 1942.
26. Fraser, F. C. and Fainstat, T. D.: Production of Congenital Defects in the Offspring of Pregnant Mice Treated with Cortisone; Progress Report. Pediatrics, 8: 527, Oct. 1951.
27. Glaubach, S.; Antopol, W. and Graff, S.: Bull. New York Acad. Med., 27: 398, 1951.
28. Robson, J. M. and Sharaf, A. A.: J. Physiol., 114: 11, 1951.
29. Seifter, J.; Christian, J. J. and Ehrich, W. E.: Federation Proc., 10: 334, 1951.
30. DeCosta, E. J. and Abelman, M. A.: Cortisone and Pregnancy. An Experimental and Clinical Study of the Effects of Cortisone on Gestation. Am. J. Obst. & Gynec., 64: 746, Oct. 1952.
31. Karnofsky, D. A.; Ridgway, L. P. and Patterson, P. A.: Endocrinology, 48: 596, 1951.
32. Sprague, R. G. et al.: Observations on Physiological Effects of Cortisone and ACTH in Man. Arch. Int. Med., 85: 199, 1950.
33. Brown, E. E.: Congenital Anomalies and Cortisone, Correspondence, J.A.M.A., 148: 1051, March 22, 1952.
34. Brown, E. E.: Cause of Congenital Defects Following Maternal Rubella; Role of Adrenals, Northwest Med., 46: 288, April 1947.
35. Engler, M.: Mongolism (Peristatic Amentia), 1949.
36. Down, J. L. H.: Observations on an Ethnic Classification of Idiots. London Hosp. Rep., 3: 259-262, 1866.
37. Crookshank, F. G.: The Mongol in Our Midst, 3rd Ed., 1931.
38. Husler, J.: in Pfaundler & Schlossmann, The Diseases of Children, Vol. 2, p. 36, 1935.
39. Graydon, J. J. and Simmons, R. T.: Rh Factor and Blood Group Frequencies in Japanese. M. J. Australia, 1: 601, June 16, 1945.
40. Howard, E. M.: Erythroblastosis Foetalis. Journal-Lancet, 65: 1, Jan. 1945.
41. Benda, C. E.: Clinical Aspects of So-Called Mongolian Imbecility. Arch. Neurol. & Phychiat., 53: 450, June 1945.
42. Mongolism and Fertility, Queries and Minor Notes. J.A.M.A., 114: 180, Jan. 13, 1940.
43. Jenkins, R. L.: Etiology of Mongolism. Am. J. Dis. Child., 45: 506, March 1933.
44. Bleyer, A.: Role of Advanced Age in Causing Mongolism. Am. J. Dis. Child., 55: 79, Jan. 1938.
45. Brown, E. E.: Mongolism and "Missed Mongolism" Following Maternal Illness. ARCH. PEDIAT., 70: 389-394, Dec. 1953.
46. Benda, C. E.: Prenatal Maternal Factors in Mongolism. J.A.M.A., 139: 979, April 9, 1949.
47. Mongolism; Some Newer Developments. Pfizer Spectrum, J.A.M.A., 152: adv. p. 23, Aug. 1, 1953.

TREATMENT OF CELIAC DISEASE WITH DIET FREE FROM WHEAT, RYE AND OATS. (Tidsskrift for Den Norske Laegeforening. Oslo, 73:695, Sept. 15, 1953). Clinical-experimental studies by a group of Dutch investigators disclosed the harmful effect of wheat, rye and oats in celiac disease. Since December 1952, diet from which these substances were excluded has been applied for from 4 to 16 weeks in the Children's Clinic of the Rigshospital in the treatment of 12 cases of verified celiac disease. Grette and Imerslund confirm the good results reported by others with the treatment. All the patients showed excellent clinical, roentgenologic, and biochemical response. The diet departs but little from the ordinary diet, is inexpensive, and can be made varied and pleasing to the taste. Its introduction is regarded as a distinct advance in the treatment of celiac disease.—*J.A.M.A.*

THE JEALOUS CHILD

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The jealous child is not an uncommon phenomenon in our culture. The jealous child is rather frequently encountered because conditions in our society are such that childhood is not always the happy, carefree, secure existence it is popularly supposed to be. Jealousy is a manifestation of many inner needs that are not or cannot be fulfilled. In many instances, it is the final, total result of physical, mental and emotional deficiencies of one sort or another.

Stated simply, a child is jealous when he wants something that someone else has, and he has not. This something may by physical, mental, emotional, economic, social, financial, etc. Jealousy, when it is not exaggerated, is normal in children as it is in adults. A jealous child will not necessarily grow up to be a jealous adult. However, jealousy in itself, is only a symptom. It can become harmful when it arouses marked disapproval in his parents and generates emotional tensions and conflicts resulting in behavior disorders.

Parents need to understand what lies back of the child's behavior. They must learn how to help him to accept his feelings of envy and jealousy without arousing a sense of guilt that may impede his progress toward full maturity. Many adults exhibit neurotic symptoms because of faulty handling of jealousy by parents when they were children.

Basically, it is the child's need for protection that makes him anxious to obtain and preserve his parents' affection, and it is this need that causes him to look with suspicion upon his brothers and sisters. According to Freudian thinking, the jealousy of an only child takes the form of the Oedipus complex. Arrival of another child causes much resentment on the part of the first born, as he feels deprived of many of his privileges. Later, the addition of a third child may give him the opportunity to take his revenge. He may form a coalition with the youngest child against the second born, who is caught in the middle.

Jealousy between brother and sister is either based upon envy of anatomical differences, or upon a misunderstanding of the differential treatment received during education.

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An unusual situation arises when there are identical twins in the family. The twins regard themselves as a unit and are regarded as such by their brothers and sisters, who may look with envy at the special attention the pair receives. As the twins realize that the strength of their position rests upon their being alike, they become anxious to enhance and preserve this likeness as long as possible. Hatred and love exist in these families to the same extent as in others and tension and confusion is said to be even greater where more sets of twins are present. Nonidentical twins usually take on an individualistic attitude toward each other.

Death of a parent is a grievous blow to the child's feeling of security. It increases his dependency on the remaining parent, and makes him even more possessive of the parent and more jealous of his siblings. There is the danger that a widowed mother, occupied with her own grief and burdened with new responsibilities, may overlook the sorrows of her children.

If a home is broken up by death or divorce, the children may find new reasons for jealousy. They will oppose any wish of the parent to remarry and, should remarriage take place, the stepparent becomes the object of jealousy. Should both partners bring their respective broods into the new household, the gates are opened wide for every form and current of envy, hatred and jealousy.

Jealousy is least developed in neglected children, simply because there is not much to be jealous of. This points to the undeniable influence which the attitude of the parents exert on the development of childhood jealousy, and thereby on the character formation of the child. Playing favorites, inconsistent discipline, overt comparison of the children—all will have a devastating effect on the children's state of mind. These practices will fan the flame of jealousy and create an exaggerated spirit of rivalry which later may result in an unsound search for power that can never be satisfied. The rôle of the parent should be that of a moderator. The children should not be told to "love" one another, as the competitive spirit cannot be eradicated completely from the family. It is the family that must prepare the child to live in our competitive society.

Jealousy is also aroused by social inequalities, by economic deficiencies and financial difficulties. Children are quick to note and observe what other children have in the way of material goods, social security and position. When they find these things desirable on others, they also desire them for themselves and, when they lack these, they become jealous.

Children also know the meaning of good health and physical perfection. They see them in other children, and when they lack these they are intensely jealous. Especially do they resist any illness which sets them apart from others, such as diabetes, epilepsy, tuberculosis, cerebral palsy; they resent any physical condition, such as harelip, facial and figure deformities, which tend to stigmatize them.

Jealousy is of instinctual origin. Its suppression would only drive it underground, with the result of a host of psychosomatic ills. Jealousy should be brought into the open and managed with frankness and honesty. Only in this way are the avenues opened for the promotion of emotional maturity.

TREATMENT OF PRIMARY INFECTION IN CHILDREN. (Pediatrie, Lyon, 8: 23, No. 1, 1953). Antibiotics are of little value in treating primary infection in the child. The lymph node lesions soon become caseous and offer ideal conditions for the development of drug resistance. The encapsulatd bacilli remain viable and may subsequently be disseminated by way of the blood or the lymph. Hasty and inadequate use of antibiotics may produce drug resistance and thus destroy the efficacy of these products in later, severe manifestations of the disease, for which they are the only effective treatment. Children under 15 years of age presenting radiological or clinical signs of initial tuberculosis, traditionally considered transient or benign, should not be placed in institutions (unless others in the family have tuberculosis) or treated with antibiotics, but should be kept under close observation for two years. Patients with severe forms of the disease, especially micronodular, should be treated at once. They may as a rule be given streptomycin for six months in combination with *p*-aminosalicylic acid for 12 months. The period of administration should not be curtailed, because the efficacy of streptomycin treatment depends essentially upon its length. Borderline cases require very careful consideration; the present tendency is toward caution in the use of antibiotics. Diagnosis should be based on the fullest possible study carried out at a hospital, and treatment must be individualized; the child's age and constitution, and the conditions of infection all modify the general indications for therapy and should be taken into account.—*Journal A.M.A.*

PEDIATRICS AT THE TURN OF THE CENTURY

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

CONGENITAL GASTRIC SPASM*

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Doubt has been expressed by some as to the existance of a true congenital hypertrophic stenosis of the pylorus. An examination of the literature and of some stomachs shown as specimens of this condition shows that two classes of cases have been described under this title. A few, a very few, cases are reported where there has been found postmortem hyperplasia of the epithelium, an increase of connective tissue in the submucosa, and of fibrous tissue in the muscular coat, in addition to hypertrophy of both the longitudinal and circular muscular layers, the presence of this abnormal tissue causing, sooner or later, a true stenosis. More cases are to be found, similar to the one here reported, where there is only found an hypertrophy of the circular muscular layer, the stenosis which undoubtedly exists being due almost entirely to spasm of the hypertrophied muscle. To the first class the title should be restricted, and to the second is better given the name suggested by Dr. John Thomson, viz.: congenital gastric spasm.

The practical importance of this distinction is lessened somewhat by the difficulty in differentiating the two conditions during life, as the symtoms are similar, and both may have a palpable tumor, gastric peristalsis, and dilation. A few cases of congenital gastric spasm have been relieved by careful diet and treatment and others have had periods of relaxation of the spasm, but it is not to be expected that cases of true hypertrophic stenosis will be permanently benefited except by surgical procedures. Since the prospect that the cases of gastric spasm will be permanently relieved by treatment or that the relaxation will remain is very small, it would

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seem best that all cases of both classes should be submitted to an early surgical operation, and especially so if a palpable tumor is present.

CASE REPORT

History of Case. The stomach here presented was taken from the body of infant Dodd, who died when thirty-two days old. With the exception of the maternal grandmother, who died with typhoid fever, the grandparents are living and well. The father, thirty-eight years old, the principal of a school, has had symptoms of pyloric spasm at times for the past four years. The mother, twenty-four years old, is not very strong and is rather nervous. During the last half of this, her second pregnancy, she suffered a great deal with burning in her stomach and eructations of a sour fluid. The only other child is a son three and one-half years old. He had colic severely and was very constipated for his first three months. Ever since then his bowels and appetite have been very irregular.

The baby, a male, was born July 12th after a normal labor and his estimated weight was ten pounds. On the next day his bowels and kidneys acted well. During the third twenty-four hours he had from fifteen to twenty large thin stools. This diarrhea stopped suddenly without apparent cause.

Vomiting. The child nursed vigorously within a half hour after his birth. The flow of milk was well established on the third day. There was retching on the first day, more on the second, and on the third day vomiting began and continued more or less until the death of the baby. The milk was usually expelled within five to thirty minutes, but a few times was retained for two or three hours and three or four times for four or five hours. The vomiting was always projectile and usually came on without warning, seldom being preceded by retching. Occasionally there was severe retching without vomiting. During the first part of the second week, when he was allowed to nurse all he wanted, he would often vomit before he was through nursing and immediately nurse again. The length of time he nursed seemed to have no relation to the length of time the milk was retained. On the thirteenth day the attending physicians made a diagnosis of ileocecal intussusception and indistinctly felt a tumor about two inches long. For the next three days (July 14th, 15th, 16th) he was given nothing by the stomach but an occasional spoonful of water and while there was no vomiting there

was a great deal of retching. For these three days rectal feeding and injections were resorted to but without improvement in the symptoms. For the thirty-six hours following the three days' fast he was allowed to nurse for two minutes every two to four hours; and, while he would vomit within two minutes to two hours, it was thought he retained more of the milk than formerly. The appearance of the vomitus varied with the length of time it was retained in the stomach, that retained the longest being the most digested. What I saw in a bottle brought to me was one-third soft milk clot and two-thirds light, straw-colored liquid. At no time was it stained with bile but contained some mucus toward the end and during the last week was a very dark brown color and of an offensive odor.

Stools. After the diarrhea on the third day there was obstinate constipation. A rectal injection was given at least once each day that usually caused a slight movement, and occasionally there was a very small passage without the injection. Four passages were shown to me; in the four there was about two teaspoonsful, nine-tenths of which was green mucus, the other one-tenth being small yellow flakes irregularly distributed through it. Thirty-six hours after his fast he had a small stool very much like a milk stool, only not so bright a yellow, and two similar ones the next day. Otherwise they were as first described until the last week when the few were the color and consistency of tar and very offensive. At no time was there a bloody or blood-stained mucous stool.

Pain. The suffering of the baby was intense much of the time. The pain would come on after nursing, with vomiting and attempts at vomiting, and even the eructation of gas was painful. A teaspoonful of hot or cold water would excite it. From the first there was pain following nursing, and in addition severe paroxysms, often lasting a half hour, that were more severe after midnight. After a few nursings on the seventeenth and eighteenth days there was little or no pain.

Physical Examination. I saw the child with Drs. Wood and Gregg, the attending physicians, on the twenty-second day. It was considerably, but not greatly, emaciated. For the previous twenty-four hours it had been having small doses of opium and belladonna and was quiet. There was but slight distention of the abdomen, limited to the upper part and most noticeable in the left half of

the epigastrium. Very slight gastric peristalsis could be seen at times but this was never prominent. Pressure on the stomach would cause a light wave of contraction and at long intervals this was felt without pressure exciting it. Standing at the side of the mother while the child nursed one could hear loud gurgling that continued, gradually growing fainter, and ceased when nursing ended. This could also be heard when there was vomiting or retching and continued throughout the illness, being more marked the last week. The abdominal walls were very soft and a swelling about one by one-half inch was easily felt one inch to the right of the median line and three-fourths of an inch below the border of the ribs. Nothing else abnormal was found.

General Symptoms. The urinary secretion was high-colored and somewhat diminished but not scanty, owing, no doubt, to rectal injections. There was no fever until the last week. The child emaciated rapidly the last few days and died on the thirty-second day after having convulsions for seventeen hours. Its estimated weight at death was five pounds.

Autopsy. This was limited to the abdomen. The stomach was full and contained some fluid and mucus. At the pylorus was found a very hard swelling one inch long and three-fourth inch in circumference. The cardiac end of the stomach (about one-third) was thin, distended, and prominent. Toward the pylorus (two-thirds of the stomach) the walls were thick and contracted. The examination of a section of the pylorus by the microscope shows only an hypertrophy of the circular muscular layer.

PAROXYSMAL HEMOGLOBINURIA*

REPORT OF CASE IN A BOY FOUR YEARS OLD

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Paroxysmal hemoglobinuria is a comparatively rare disease in children. Only about 20 cases have been published. I therefore consider the following case worthy of being reported.

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*Read before the Section on Pediatrics, New York Academy of Medicine, January 8 1903.

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Family History. The patient is a boy four years and three months old. The parents have been married six years. Four years before marriage the father had syphilis. He was treated for one year with internal medication. The patient is the only child. The mother has had no miscarriages. The labor was normal.

Personal History. At four months of age the patient presented undoubted signs of congenital syphilis. The mother says that the child looked peculiar at that time. He had snuffles, keratitis, and an eruption on the genital region; the soles of the feet were red and shiny, with peeling of the skin; there were rhagades around the mouth. The child was treated for one year with mercury. Marked improvement immediately followed and all the syphilitic manifestations disappeared. At three years he had measles; at four, whooping-cough without complications.

Present History. The patient first came under observation on November 14, 1902. He had had attacks of hemoglobinuria during the previous four weeks, sometimes two in one day, latterly three or four a week.

Examination. The patient is somewhat undersized, his height is three feet two and one half inches; weight, thirty-two pounds, fourteen ounces. He is anemic. The root of the nose is not depressed. The scars of the fissures about the mouth are still visible. The teeth are carious. A hemic murmur is heard in the neck. The heart and lungs show nothing abnormal. The liver is not enlarged. The spleen can be felt 3 cm. below the free border of the ribs in the anterior axillary line. The appetite is poor, the bowels regular. Examination of the blood shows no plasmodia.

The attacks of hemoglobinuria usually come on about ten o'clock in the morning. While playing the child becomes peevish and irritable, yawns several times, rubs his forehead, and complains of pain in the head. A chill then sets in, the lips become blue, the face pale, the legs like marble. He then says that he feels tired and wishes to lie down. After sleeping for half an hour, during which time the temperature rises, and the skin assumes its normal red color, he passes a quantity of reddish brown urine and feels very much better. The next urine voided is only slightly colored, with a marked deposit of urates. During an attack the mother has never noticed any edema or any purpuric or urticarial eruption. The entire attack lasts for an hour to an hour and

a half. The mother does not think that exposure to cold or walking brings on an attack.

November 14. The patient is put on "mixed treatment."

November 18. The patient has another severe attack lasting an hour and a half.

November 23. A mild attack, while playing. There is slight cyanosis, but no chill; he does not wish to lie down. After the attack he passes a quantity of reddish brown urine.

November 27. He has a chill with cyanosis, vomiting and fever, after which he sleeps. The day preceding this attack the child received a lukewarm water bath. While in the bath he had a slight chill. This undoubtedly brought on the attack.

December 8. A slight attack.

December 28. He has had no attack since December 8. The spleen can no longer be felt below the free border of the ribs. Hemoglobin, 45 per cent. (Fleischl).

The urine examined following the attack of November 13th showed: Color, reddish brown (the same as solution of bismarck brown), with a brown sediment; acid reaction; specific gravity, 1030. Albumin, 3½ per cent.; (Esbach) no sugar; no indican. Heller's test is positive, with the characteristic deposit, the urine above becoming clear yellow. Hemin crystals are easily obtained by the usual method.

Microscopically there are no red corpuscles, no shadows; a few hyaline and granular casts, and pigment granules. An examination of the urine following the attack of November 18th gives substantially the same results.

Etiology. The sexes are about equally affected. The age of the onset of the attacks varies from nine months to nine years. A distinct history of congenital syphilis is present in about one half the cases. The attacks may be brought on by exposure to cold, not, however, by the eating of cold articles of food, such as cold drinks and ices. The attacks may be produced artificially by cold baths or often by simply immersing one of the extremities in cold water. Physical exertion or emotional shock is also a predisposing cause.

Pathology. In a case described by Dieulafoy and Widal, the patient died during the attack. The cortical portion of the kidney was found at the autopsy to be of a dark brown color. Microscopically the glomeruli were normal; the cells of the convoluted

tubules and the ascending limb of Henle's loop showed an infiltration with pigment granules, even in the lumen of the tubes.

In Heidenhain's experiment, indigo injected into the general circulation was also deposited in this portion of the kidney. This would give support to the generally accepted theory that the hemoglobinuria is preceded by the presence of hemoglobin in the circulating plasma, that is, by hemoglobinemia.

Pathogenesis. In the production of attacks of paroxysmal hemoglobinuria there are two important factors. First, changes in the blood; second, an increased irritability of the vasomotor system. According to the investigations of Ponfick hemoglobin may enter the circulating plasma in one of two ways, either the red blood corpuscles are broken up and gradually destroyed, setting free their hemoglobin, or the hemoglobin is dissolved directly out of the red blood corpuscles, leaving only the framework as a shadow. He has also shown that, for the production of hemoglobinuria, it is necessary that a certain amount of hemoglobin (which he estimates at one-sixtieth of that present in the entire body) should be set free within a comparatively short time.

Among the first to perform experiments on the blood of a patient with hemoglobinuria was Ehrlich. He found that when a ligature was placed around the finger, and cold applied to the part, in the blood drawn the serum, which separated from the clot, was red instead of pale yellow; that is, a hemoglobinemia had been produced. Chvostek found that circulatory disturbances without the application of cold produced the same result, and also that the blood corpuscles of the patient were less resistant to the action of mechanical influences, such as shaking. Luzzatti and Sorgente repeated these and made several additional experiments.

The first set of experiments was made in vitro with the blood of the patient obtained in the interval between attacks. The conclusions drawn were:

(1) Cold has no direct effect on the blood of the patient.

(2) The corpuscles show no diminished resistance to the effect of cold.

(3) The corpuscles are destroyed by suddent changes of temperature.

(4) The corpuscles show no diminished resistance to the effect of mechanical influences.

(5) An increased quantity of CO_2 in the blood probably favors the dissolution of the red blood corpuscles.

The second set of experiments was performed by placing a ligature around the arm of the patient with and without the simultaneous application of cold to the extremity. The conclusions drawn were:

(1) The congestion producted by the ligature also causes a distinct cooling of the part.

(2) No hemoglobinemia is produced, when the congested part is artificially kept warm.

(3) The most marked hemoglobinemia is produced by the combined action of the ligature and cold.

(4) Cold has a direct action on the circulating blood.

(5) The serum of the blood in the intervals between attacks has no hemolytic action; on the contrary, that obtained from the blood of the extremity to which the ligature and cold have been applied has a distinct and rapid hemolytic effect.

I have repeated some of these experiments so far as the age and the fact that the patient was not in the hospital would permit.

For the examination of the blood the small spindle shaped capillary tubes used for obtaining the serum for the Widal reaction were found very convenient.

The microscopical examination of the blood of the patient, obtained between the attacks, showed no changes except those of a simple anemia. The application of cold to the blood in the capillary tube produced no change in the clotting; the serum which separated was pale yellow; microscopically examined the red blood corpuscles were found unaltered.

An elastic ligature was placed around the index finger and the hand a part of the forearm were placed in water at 45° F. for ten minutes. The hand, especially the index finger, became swollen and cyanotic. When the finger was punctured the blood at first flowed very slowly, afterward much more freely. Clotting took place in the usual way, but the serum which separated was red. In the second tube, which contained blood obtained after the circulation in the finger was again normal, the serum was yellow.

To the red corpsucles obtained from this last tube, serum from my own blood was added. No changes could be observed microscopically in the corpuscles. On the other hand when the patient's

serum was added to my own red corpuscles it became red within a short time. Microscopically a great many shadows were seen, showing that the hemoglobin had been dissolved out of the corpuscles.

It seems probable that the syphilitic poison may produce in the plasma substances which under certain conditions have a hemolytic action. We already know that a number of bacteria in cultures produce such substances.

The study of the hemolysins is of comparatively recent date. All that is definitely known concerning these substances will be found in Welch's recent Huxley lecture.

Prognosis. It is remarkable how quickly the patient recovers after what appears to be a very severe attack. In an hour or two he is playing about, as if nothing had happened. Even if the attacks are frequent, there seems to be no danger to life. With the exception of the anemia, which is sometimes marked, the general condition of the patient does not seem to suffer. In those cases in which there is a history of syphilis, the administration of mercury and the iodids cause a rapid improvement in the general appearance and in the character of the blood. The attacks are apt to recur, especially in winter, and may continue for a number of years. In many cases occurring in adults the disease dates back to early childhood. In giving a favorable prognosis the possibility of the development of nephritis must be borne in mind.

Treatment. In the syphilitic cases specific treatment almost always causes an amelioration in the severity and in the frequency of the attacks. A very good method, as I have found, is to give the patient alternately for five days the protiodid of mercury, from 1/20 to 1/10 grain, three times a day, and for five days the peptonate of iron. Even in cases in which there is no distinct syphilitic history or manifestations, it is best to give the patient the benefit of the doubt. Where there is a history of malaria, quinine is indicated.

The diet of the patient should be regulated, and large quantities of milk and of water given, so that the kidneys will be thoroughly flushed and freed from any deposit of pigment which might obstruct the urinary tubules. When the urine contains an abundance of urates, alkalies should be given. For the improvement of the general condition tonics and cod liver oil are indicated. When the

attacks are frequent, the patient should be kept perfectly quiet; walking should be especially forbidden.

Great care should be taken to prevent any exposure to cold. During the winter months, except on days on which the temperature is not low, the child should remain in the house. No cold baths should be given.

Chvostek succeeded in cutting short an attack in a patient by giving inhalations of amyl nitrite, which rapidly dilates the blood vessels. As the contraction of the cutaneous blood vessels probably plays an important part in causing an attack, it would seem rational to give the patient a hot mustard bath with friction of the skin, as soon as the first symptoms of an oncoming attack are noticed.

In order to increase the resistance of the blood vessels of the skin to the effects of exposure to cold, warm baths with friction of the skin will be useful. The temperature of the water can be gradually lowered each day. At the first signs of a chill the patient should be removed from the bath and the next baths given at a slightly higher temperature.

CONGENITAL ABSENCE OF TEAR SECRETION. (Klin. Monatsbl. für Augenheilkunde, Stuttgart, 122:554, No. 5, 1953). Sjögren reports 14 cases of congenital absence of tear secretion which he found recorded in the literature, beginning with the first case described by Morton in 1844 and ending with a case observed by himself and Eriksen in 1950. The condition is usually of neurogenic origin, that is, it is due to aplasia of the secretory nuclei, or to the fact that connection between the secretory center and the nerve tracts is lacking now and then in newborn infants. It may be caused by a congenital disturbance in the autonomic nervous system. It is possible that in a few cases aplasia of the lacrimal glands exists. This has not been definitely proved, but if such cases do occur they may perhaps be incomplete forms of congenital ectodermal dysplasia. Thus there seems to be a congenital form of keratoconjunctivitis sicca which differs fundamentally from the form which occurs in adults: in infants there is aplasia, in adults, atrophy.— *Journal A.M.A.*

The magic whispers...

When Grandpa tucked you between his knees, you knew you were going to listen again to his wonderful watch—to hear its magic tick . . . tick . . . tick . . .

And as you listened, those measured whispers of time shut away the world, leaving you close to Grandpa, secure in his love.

From fathers and mothers to sons and daughters passes the lifeblood of happiness—security. The privilege of providing it for those we love can be found only in a land like ours.

And another wonderful thing is this: By realizing this privilege of freedom for ourselves, we achieve the security of our country. For, think—the strength of America is simply the strength of one secure home touching that of another.

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